UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/534,509	03/24/00	TKACHUK	Z 000152

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HM12/0626

EXAMINER	
DRABIK,C	
ART UNIT	**PAPER NUMBER**
1633	3

DATE MAILED: 06/26/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev.11/00)

1- File Copy

Manual of Patent Examining Procedure, Section 713.04 Substance of Interview must Be Made of Record

A complete written statement as to the substance of any face-to-face or telephone interview with regard to an application must be made of record in the application, whether or not an agreement with the examiner was reached at the interview.

§1.133 Interviews

* * * * *

(b) In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for response to Office action as specified in §§ 1.111,1.135. (35 U.S.C.132)

§ 1.2. Business to be transacted in writing. All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete a two-sheet carbon interleaf Interview Summary Form for each interview held after January 1, 1978 where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks in neat handwritten form using a ball point pen. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below.

The Interview Summary Form shall be given an appropriate paper number, placed in the right hand portion of the file, and listed on the "Contents" list on the file wrapper. The docket and serial register cards need not be updated to reflect interviews. In a personal interview, the duplicate copy of the Form is removed and given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephonic interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the telephonic interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Serial Number of the application
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (personal or telephonic)
- Name of participant(s)) (applicant, attorney or agent, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the claims discussed
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). (Agreements as to allowability are tentative and do not restrict further action by the examiner to the contrary.)
- The signature of the examiner who conducted the interview
- Names of other Patent and Trademark Office personnel present.

The Form also contains a statement reminding the applicant of his responsibility to record the substance of the interview.

It is desireable that the examiner orally remind the applicant of his obligation to record the substance of the interview in each case unless both applicant and examiner agree that the examiner will record same. Where the examiner agrees to record the substance of the interview, or when it is adequately recorded on the Form or in an attachment to the Form, the examiner should check a box at the bottom of the Form informing the applicant that he need not supplement the Form by submitting a separate record of the substance of the interview.

It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner. The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he feels were or might be persuasive to the examiner,
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Stimmary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete or accurate, the examiner will give the applicant one month from the date of the notifying letter or the remainder of any period for response, whichever is longer, to complete the response and thereby avoid abandonment of the application (37 CFR 1.135(c)).

Examiner to Check for Accuracy

Applicant's summary of what took place at the interview should be carefully checked to determine the accuracy of any argument or statement attributed to the examiner during the interview. If there is an inaccuracy and it bears directly on the question of patentability, it should be pointed out in the next Office letter. If the claims are allowable for other reasons of record, the examiner should send a letter setting forth his or her version of the statement attributed to him. If the record is complete and accurate, the examiner should place the indication "Interview record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

*U.S. GPO: 1997-422-310/60005

Office Action Summary	Application No. 09/534,509	Applicant(s) TKACHUK, ZENOVIY	
	Examiner Christopher Drabik	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-22 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-22 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other:

DETAILED ACTION

Specification

The disclosure is objected to because of the following informalities: The specification has numerous errors in regards to spelling, punctuation, scientific notation, and usage. For example, commas and periods seem to be randomly used in scientific notation. (see e.g. page 30). The critical analysis of experimental details is at times hindered by imprecise description. For example, on page 32 an experiment is disclosed in which the concentration of nucleic acid is given as 10 or 100μg. No volume for the reaction is given, therefore, there is no way of knowing what is the actual concentration of nucleic acid in the reaction.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6-19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites: "A method for the treatment of inflammation...comprising administering to a mammal...an amount effective to ameliorate the symptoms of inflammation or inflammatory-related disorder of ribonucleic

acid ..." This claim is vague and indefinite because it is unclear what is being administered in an effective amount. Furthermore the claim can be read as meaning that the inflammation or inflammatory related disorder is caused by or associated with ("of") ribonucleic acid. Claims 6-19 depend from claim 1 and are bound by the limitations of claim 1. Hence claims 6-19 are also rejected for being vague and indefinite.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 2 is vague and indefinite because it is not clearly pointed out what is administered in an effective amount such that membranes are stabilized.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 3 is vague and indefinite because it is not clearly pointed out what is administered in an effective amount such that oxidation of membrane components is inhibited.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 is vague and indefinite because it is not clearly

pointed out what is administered in an effective amount such that NO synthetase activity is "normalized."

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 recites " A method of normalization of NO-synthetase..." It is unclear what the applicants mean by "normalization." The implication of the claim is that the enzymatic activity (i.e. the mechanism by which the enzyme biochemically acts to produce NO) is in some way changed such that it is returned to normal functioning, however, it is not clear how the enzymatic mechanism of NO-synthetase is altered in vivo. It is also unclear under what circumstances the enzymes catalytic mechanism may be abnormal.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 5 is vague and indefinite because it is not clearly pointed out what is administered in an effective amount such that thrombocyte aggregation is inhibited.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,6-19 are rejected under 35 USC112, first paragraph, because the specification, while being enabling for the treatment of acute inflammatory events involving short term effects, wherein the ribonucleic acid is total yeast RNA, wherein the RNA is injected interabdominally, wherein the administration of the RNA is prior to the inflammatory event, the specification does not reasonably provide enablement for total RNA extracted from other sources, is not enabled for chronic inflammatory diseases and is not enabled for routes of administration other than interabdominal injection.

Claims 1 and 6-19 are broadly drawn to a method of treating or reducing inflammation in mammals. The claimed method involves the administration of ribonucleic acid wherein the ribonucleic acid has the effect of reducing or treating inflammatory events. The scope of the claims encompass any form or type of ribonucleic acid. This includes at least single stranded RNA, double stranded RNA, RNA with modifed or atypical bases, ribozymes and single ribonucleotides. The RNA can be from any source. The administration of the RNA is not limited to any particular method. The claims are drawn to the treatment of any form of inflammation or inflammatory related disorder. The scope of the diseases claimed, therefore, includes a large group of related and unrelated human diseases. Virtually any disease state which causes an immune reaction can be associated with inflammation. Hence, the scope of the claims includes widely varying mammalian afflictions, including autoimmune diseases, asthma, bacterial and viral infections.

While the breadth of the claims are broad, the nature of the disclosed invention has to do with the administration of total RNA from yeast to an individual suffering from

inflammatory or inflammatory related disorder. The administration of total RNA to a patient for ameliorative or curative benefit of a disease has little precedent in the art. Although applicant asserts that nucleic acids are commonly used in pharmacology (see page 12), the applications of nucleic acids cited involve nucleic acids with specific sequences which target well defined cellular targets and have a defined mechanism of action. The effects of the in vivo administration of total RNA of any organism to another organism resulting in the amelioration of a disease state has not been well documented. The examples provided by the applicant, therfore, must take on considerable weight when analyzing the scope of enablement of the claims.

Applicants have provided examples using mouse or rat animal models involving chemically induced inflammation, or induced infarction. The route of administration in all experiments was via interabdominal injection. The scope of the claimed invention, however, encompasses any form of administration. The fate of RNA administered by other means cannot be readily extrapolated from the experiments provided. For example, it is unclear whether RNA adminstered orally would be capable of surviving the enzymatic and acidic environment of the stomach such that the it could effect an inflammatory process. A hypodermally administered RNA would likley be degraded by RNAses present in the skin.

A further aspect of the experimental design of the instant application has to do with the fact that inflammatory processes were only observed when RNA was administered prior to insult. So, the data can only be interpreted in terms of preventative effects, but not ameliorative effects in an The mechanism of action of the RNA has not

been fully established and therefore the assumption of the RNAs ability to effect inflammation after the inflammatory insult has occurred (administration of RNA post insult) cannot be made. The experimental data provided by the applicants seems to indicate that the effect of RNA has only a short term effect in reducing several indices of inflammation. For example, the activity of NOS in mouse blood taken from mice treated with carageenan was maximally effective at 60 minutes, however, at 320 minutes no apparent reduction in NOS was apparent.

It is also unclear as to whether the indices for inflammation cited are sufficient to justify the assertion that all forms of inflammation can be treated by yeast RNA. For example in the adjuvant arthiritis mouse model provided as an example of chronic inflammation, the only relevant index scored is NO synthetase activity. Multiple mechanisms are involved in chronic inflammatory events and it cannot be asserted that the reduction of a single factor in chronic inflammation is predictive of a curative benefit.

Based on the limited prior art, the breadth and nature of the claims, the lack of working examples regarding routes of administration, the limited experimental evidence provided for indicating the long term effects, the limited experimental data regarding indices of inflammation, the invention is not enabled commensurate with the scope of the claims.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the in vitro stabilization of acid challenged erythrocyte plasma membranes isolated from carageenan treated rats which have been interabdominally injected with total *S. cerevisiae* RNA, does not reasonably provide enablement for the stabilization of cell membranes in vivo, other types of cell membranes or destabilization of cell membranes wherein the destabilization caused by means other than reduced pH. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The nature of the invention has to do with the administration of RNA to a mammal such that membranes are stabilized. The scope of the claims encompasses all types of membranes found in all cell types within a mammal. Implied in the scope of the claims is stabilization of membranes damaged by all forms of insult.

The direct evidence provided by the applicants for the stabilization of damaged membranes has to do with in vitro testing methodologies in which erythrocytes are challenged with acid lysis. The in vitro experiments comprise the addition of HCl to erythrocytes harvested from rats treated with carageenan or Freunds adjuvant. In test animals, total yeast RNA was administered inter-abdominally prior to the administration of chemical insult.

While it appears that membranes of erythrocytes are stabilized in the presence of acid challenge experiments, conclusions based on the stabilization of other membranes, particularly membranes at the site of inflammation cannot be directly drawn.

Erythrocytes are a specialized class of cells having different plasma membrane constituency with regard to protein and phospholipid content from other types of cells. For example, the phopholipid content of eryhthrocytes are known to differ markedly to the phopholipid content of nerve or liver cells. Furthermore, internal cellular membranes such as those present in the nucleus and mitochondria differ significantly from erythrocyte plasmas membranes. It is unpredictable how all other cell types would react to the pH under the conditions as employed in the instant application. Since the membranes of different cells have different components it is not apparent that generalizations based on erythrocyte membranes can be broadly drawn to encompass all cell types. Extrapolation of the results to predict the effects of other forms of total RNA or routes of administration other than inter-abdominally cannot be clearly made, as noted above.

In addition, the scope of the claims includes the stabilization of biologic membranes under all forms of stress. This includes lysis due to viral infection or cellular processes such as apoptosis. The in vitro demonstration of resistance to acid lysis of eryhtrocytes clearly does not mirror the processes involved in these forms of membrane destabiliazation, and hence it has not been demonstrated that the disclosure is sufficient to enable the scope of the claimed invention in regard to all forms of membrane destabilization.

Claim 3 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the inhibition of phospholipid oxidation wherein the oxidation

product is arachidonic acid, wherein the ribonucleic acid is total RNA from S cerviseae and the RNA is adminstered interabdominally , wherein the mammal is a rat or a mouse does not reasonably provide enablement for the oxidation of all cellular membrane components, for nucleic acids other than said S.cerviseae total RNA, mammals other than mice or rats or for modes of administration other than interabdominally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 3 is broadly drawn to the prevention of oxidation of all components of membranes in mammalian cells. This includes all cell types and intercellular membranes as well. The experimental examples provided in the disclosure of the instant application involve largely the measurement of arachidonic acid and metabolites of arachidonic acid. An assumption of the claims is that all forms of membrane oxidation are represented by the production of arachidonic acid. Protein and phospholipid constituents of membranes are, however, oxidized to form other breakdown products, and, therefore, modeling membrane oxidation on arachidonic acid metabolites does not provide a complete measure of all processes of membrane oxidation.

As discussed above, little precedent for the administration of total RNA is extent in the literature, and it is unclear whether any other forms of total RNA would be capable of acting in the same manner as total yeast RNA. Further, the only demonstrated route of administration is inter-abdominally and, as pointed out earlier, the

fate of total RNA administered by other routes cannot be readily predicted. Hence, the claims can only be enabled for total yeast RNA injected inter-abdominally.1

Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 4 is drawn to a method for the normalization of NO synthetase activity in mammalian cells. The nature of the invention has to do with the administration of total yeast RNA to a mammal. The extent of the experiments provided involves the measurement of NO synthetase activity in animals which have been challenged with carageenan or Freunds adjuvant.

The scope of the invention is broadly drawn to the administration of any form of ribonucleic acid to any mammal. The claim is drawn to the **normalization** of NO synthetase activity. Normalization, in general usage, means, within the context of the claim, the reduction of aberrantly elevated levels of NO synthetase activity to levels which are present in an animal before challenge. The experimental evidence provided by the applicant does not consistently support this assertion. For example in the experiment summarized in table 6, at the 320th minute of the experiment, NO synthetase activity in mice treated with RNA was at a level roughly six-fold higher than in mice not treated with carageenan. In mice injected with carageenan, there was essentially no difference in RNA treated and untreated mice at 320 minutes. In another

experiment involving rat heart ischemia (table 11), in as far as the experiment can be analyzed based on the statistical significance of the data (p-values), NOS was recorded as being approximately 15-20% higher in RNA treated rats as compared to rats not experiencing ischemia. In the same experiment, virtually no difference was seen in the combined (border and infarction zones- together) values of RNA treated and untreated animals. While other experiments seem to indicate that NOS activity may be reduced upon administration of total yeast RNA, the experiments cited above do not allow a clear and unequivocal conclusion that yeast RNA has the ability to normalize NO synthetase activity. Given that there are contradictory data in mice and rats, it would be difficult to assume an effect in other mammals.

Given that little precedent exists in the art for the administration of total yeast RNA to mammals and the contradictory data provided by the applicant, one of skill in the art is not enabled for the reduction of NO synthetase in mammals commensurate with the scope of the claims

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim1,6, 10-12, and 14 -22 rejected under 35 U.S.C. 102(b) as being anticipated by Sullivan et al.

Claims 1-22 are broadly drawn to the administration of RNA to a mammal for the ameliorative treatment of inflammation and inflammation related disorders. The scope of the RNA within the limitations of claims includes at least: single stranded RNA, double stranded RNA, ribonucleic acid with non-typical bases, ribonucleic acids with modified bases, ribozymes and single ribonucleotides. The routes of administration encompass all types of administration. The composition of the RNA formulation is recited as comprising a pharmaceutically acceptable vehicle, carrier or diluent. This encompasses a large number of possible formulations including simple diluents such as PBS, but also including delivery vehicle such as liposomes. The disease states encompassed by the invention of the instant application are recited as "inflammation and inflammatory-related" disorders. This recitation encompasses a large group of related and unrelated human diseases. Virtually any disease state which causes an immune reaction can be associated with inflammation. Hence, the scope of the claims includes widely varying mammalian afflictions, including autoimmune diseases, asthma, bacterial, and viral infections. It is further noted that the amelioration of symptoms recited in claim 1 does not necessarily mean that the inflammation per se is treated, but rather the treatment of the root disease state is also claimed, since the treatment of the disease itself will inherently reduce inflammation. For example the treatment of RSV causing inflammation in the lungs may be treated by an antiviral, which reduces the viral infection and also the related inflammation.

Sullivan et al describe ribozymes disclosed as useful for the treatment of disorders which have inflammatory components (WO94/02595). Specifically ribozymes targeting genes involved in the inflammatory process are disclosed (see Claims 1 and 2). Sullivan et al further claim a method for treating inflammatory diseases using the ribozymes (see Claim11). Ribozymes are ribonucleic acid molecules and in the disclosure of Sullivan et al they are taught as useful for the amelioration of inflammatory related symptoms, hence the limitations of Claims 1 and 20 of the instant application is clearly anticipated. Sullivan et al disclose a range of use for the ribozyme of between 100 –200 mg per Kg of body weight clearly anticipating the recited range of claim 6. The ribozymes of the Sullivan application apparently fall within the ranges of nitrogen and phosphorus content recited in Claims 10,11 21 and 22, hence, these claims are also clearly anticipated. Sullivan discloses that stenosis is an envisioned target of the ribozymes disclosed. Stenosis is a component of stroke and of cardiac infarction, therefore Claim 13 and 14 are clearly anticipated. Arthritis is particularly disclosed as a target of the ribiozymes disclosed (see Sullivan, Claim 11) Allergy has an inflammatory component. Pain, fever and swelling are by-products of an inflammatory reaction which would be addressed as the result of treating inflammation. Hence, claims 16-19 are anticipated by Sullivan et al

Claim 20-22 rejected under 35 U.S.C. 102(b) as being clearly anticipated by Tait et al (Clinical Cancer Research (1997) 3:1959-1967.)

Claims 20-22 are broadly drawn to a pharmaceutical composition comprising ribonucleic acid and a pharmaceutically acceptable vehicle, carrier, or diluent. The scope of the claim encompasses any ribonucleic acid and any pharmaceutically acceptable vehicle. As noted earlier, this includes gene delivery vehicles.

Tait et al disclose a retrovirus comprising ribonucleic acid for the in vivo treatment of breast cancer. The authors disclose a delivery vehicle consisting of ribonucleic acids encapsidated in a viral particle. (see e.g. paragraph bridging page 1960-1961) Hence the limitations of a pharmaceutical composition comprising a ribonucleic acid and a delivery vehicle are clearly anticipated by Tait et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-5, rejected under 35 U.S.C. 103(a) as being unpatentable over Sullivan et al(WO94/02595).

Claims 3-5 are drawn to methods of effecting inherent properties of inflammation. As the applicants point out in the specification, the release of arachidonic

acid (membrane oxidation), increased levels of NO synthetase and thrombocyte aggregation are all indices of inflammation. Each of these processes would be effected by treating the source of inflammation (i.e infection), or alternatively, any means for effecting one of the components of inflammation would effect the others. Hence the use of the ribozymes disclosed by Sullivan would have the inherent property of decreasing NO synthetase activity, decrease the release of arachidonic acid and reduce thrombocyte aggregation.

Conclusion

No claim of the instant application is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher Drabik whose telephone number is 703-605-1156. The examiner can normally be reached on Monday-Friday from 9am to 5pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on 703- 305-4051. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Inquiries of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-

1234. Questions regarding review of formality issues may be directed to Kim Davis, the patent analyst assisting in this application. She may be reached at 703-305-3015.

DEBORAH J. R. CLARK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600